REMARKS

This paper is submitted in response to the Office Action mailed on May 26, 2004. Claims 1-6 are pending. Claims 1-6 are rejected under 35 U.S.C. § 101 as lacking utility.

1. Information Relating to Deposit

Applicants are required, by the Examiner, to fill in the blanks in the specification indicating the ATCC accession numbers at page 15. Applicants assert that such amendment is not necessary because these amendments were already made in a Preliminary Amendment submitted with the original papers filed in this application (copy attached, Exhibit A). The vectors disclosed at page 15 of instant application were deposited with the ATCC on May 19, 1998 in accordance with the Budapest Treaty. This deposit was prior to the filing date of the parent U.S. Application Serial No. 09/083,290, filed May 22, 1998; A copy of the ATCC International Patent Depository Form, dated June 24, 1998, acknowledging receipt of the deposited vectors was filed at the Patent Office in an Amendment mailed March 11, 2004 (copy attached, Exhibit B). In addition, the parent application has been amended to incorporate said accession numbers in the specification.

Applicants believe that since the deposit was made prior to the filing date of the parent application U.S. Application Serial No. 09/083,290, under the Budapest treaty, no new matter is introduced as a result of insertion of the ATCC Accession number. As can be seen from the Deposit Receipt, the ATCC agreed to maintain the deposited plasmids for 30 years and

inventor Stuhlmann agreed to replace the materials if they become non-viable. Applicants believe no further showing is necessary and request that the objection be removed.

2. The Claims have Patentable Utility

Claims 1-6 are rejected under 35 U.S.C. §101, the examiner contending that the claimed invention lacks patentable utility. According to the Examiner, the specification states that the DB1 gene is expressed in human blood cells and adult organs but the function of DB1 protein is unknown, and the specification states that the Vezf1 gene is 98% homologous to DB1 but does not compare this with any other protein of known function. As a result, contends the Examiner, the function of either DB1 or Vezf1 protein product could not be determined with any certainty from the instant specification even if DNA claimed in the instant invention could be used to make protein. The Examiner concludes that, both the DB1 and Vezf1 genes, proteins or expression vectors claimed in instant application do not have a readily apparent utility.

Applicants respectfully disagree. An invention has a well-established utility if (1) a person of ordinary skill in the art would immediately appreciate that the invention is useful based on the characteristics of the invention (e.g. properties or application of a product or process), and (2) the utility is specific, substantial and credible. Furthermore, an applicant need only provide one credible assertion of specific and substantial utility for each claimed invention to satisfy the utility requirement.

The relevant inquiry here is whether the *Vezf1* gene and gene products have patentable utility. A mere comparison with DB1 and its gene products or absence of homology with a gene of known function does not preclude utility of the *Vezf1* gene and its gene products disclosed in the specification.

Utility of the Vezf1 gene and gene product is clearly established on the basis of it being an endothelial cell marker (page 7, lines 11-13), its use in the development of animal models for angiogenesis (page 8, lines 1-6), its use as a diagnostic tool for vascular disorders (page 7, lines 14-21), and its use in the treatment of vascular disorders (page 8, lines 7-11). A person of ordinary skill in the art would immediately appreciate that the utilities described in the instant claims are supported by the pattern of Vezf1 expression in proliferating endothelial cells found in capillary networks and mature vessels (Figures 9-12; page 41, line 8 to page 43, line 11).

A published article entitled: "Vezf1:A Zinc finger transcription factor restricted to endothelial cells and their precursors" by Xiong et al., (Dev Biol. 1999. 206:123-141) peer-reviewed by persons skilled in the art, determined that evidence presented in the manuscript support a role for Vezf1 in the endothelial lineage and during later stages of embryonic vasculogenesis and angiogenesis. This published article provides support for the specific functional attributes of Vezf1, by describing the marker gene characteristics for endothelial cells claimed in the instant application. Similarly, an article entitled: "Vezf1/DB1 is an endothelial cell-specific transcription factor that regulates expression of the endothelin-1 promoter" by

Aitsebaomo et al., J Biol Chem. 2001, 276:39197-39205, demonstrates the nuclear localization of Vezf1 and endothelial cell specific transactivation of the endothelin-1 promoter by Vezf1. This supports its role as an endothelial cell specific Zinc-finger containing transactivator.

The Examiner has further alleged that Applicants do not provide a reasonable correlation between Vezf1 expression and endothelial cells. He cites several instances in the specification which according to his interpretations support this contention of lack of correlation between Vezf1 expression and endothelial cells.

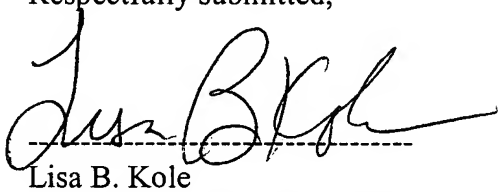
Applicants respectfully disagree. Peer reviewed publications Xiong et al., Dev. Biol. 1999. 206:123-141 and Aitsebaomo et al., J Biol Chem. 2001, 276:39197-39205 indicate that those of ordinary skill in the art accept the endothelial cell specific expression of Vezf1. Additionally, a previously submitted Declaration of Dr. Heidi Stuhlmann (the "Stuhlmann Declaration") provides support for endothelial cell specific expression of Vezf1. The Examiner has contended that the Stuhlmann Declaration cannot be found. The Stuhlmann Declaration was originally submitted in the parent application (U.S.S.N. 09/083,290) on January 17, 2002 under Express mail certificate EF377398715US. A copy of the Stuhlmann Declaration was then filed in the present application on March, 15, 2004 (copy attached, Exhibit C).

The HER-2/neu gene was first discovered and reported in the context of human breast cancer. It is currently used on an extensive basis as a diagnostic and prognostic marker in human breast cancer. Innumerable scientific publications and clinical studies however also report the utility of HER-2/neu in human prostate, ovarian, endometrial, osteosarcoma, parotid gland

and other cancers. Despite these more recent findings the validity of the HER-2/neu in the breast cancer context still holds as an accepted standard. The Examiner is of the view that there is lack of correlation between Vezf1 expression and endothelial cells and that other cell types may also express this gene. There is however clearly demonstrable utility of *Vezf1* as an endothelial cell specific marker, based on evidence provided in the instant application and supported by peer reviewed scientific publications. The Applicant's therefore respectfully traverse the Examiner's rejections and contend that the *Vezf1* gene and gene products have clear and demonstrable patentable utility.

For all the foregoing reasons, the present invention satisfies the requirement for credible utility under 35 U.S.C. §101. It is respectfully requested that rejections of the claims be withdrawn. An early allowance is earnestly requested.

Respectfully submitted,



Lisa B. Kole
Patent Office Reg. No. 35,225

Baker Botts L.L.P.
30 Rockefeller Plaza
New York, NY 10112
(212) 408-2500

Attorney for Applicants

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Stuhlmann et al.

Serial No.: (to be assigned)

Filed : January 17, 2002

For : VASCULAR ENDOTHELIAL ZINC FINGER 1 GENE AND PROTEIN AND USES THEREOF

PRELIMINARY AMENDMENT

VIA EXPRESS MAIL Label No. EF377398715US

Assistant Commissioner for Patents
Washington, DC 20231

Sir:

Preliminary to examination of the accompanying above-captioned application, applicants respectfully request consideration of the above-captioned application amended as follows:

AMENDMENTS

IN THE SPECIFICATION:

At page 1 above the heading INTRODUCTION, please insert the following heading and paragraph:

-- CROSS REFERENCE TO RELATED APPLICATIONS

This application is a continuation application under 37 C.F.R. § 1.53(b) of continued prosecution application (CPA) filed July 5, 2001 of application Serial No. 09/083,290 filed May 22, 1998. --

Please replace the paragraph beginning on page 14, line 16 and ending on page 15, line 2 with the following paragraph:

-- Two purified and isolated nucleic acids, together comprising *Vezf1* cDNA, termed *mVezf1.1* (3-1444) and *mVezf1.2*(1394-2820), containing nucleic acid residues 3-1444 (in a 1.444 kb EcoRI-EcoRI cDNA fragment) and 1394-2820 (in a 1.429

kb EcoRI-EcoRI cDNA fragment) of murine *Vezf1* cDNA, respectively, in pBluescript II SK (grown in DH5ÿ) and a nucleic acid, termed *mVezf1.N*, containing the aforementioned 20 kb genomic NotI-NotI fragment in pBluescript II SK (grown in DH5ÿ) , have been deposited under the terms of the Budapest Treaty with the American Type Culture Collection (ATCC), having an address of 12301 Parklawn Drive, Rockville, Maryland, 20852 on May 19, 1998 and assigned accession nos. 209873, 209874, and 209875, respectively. --

IN THE CLAIMS:

Please cancel claims 7-25 without prejudice to the prosecution of this subject matter in separate patent applications.

REMARKS

Prior to the examination of the above-captioned application, applicants respectfully request that the above amendments be made of record and the remarks made herein be considered by the Examiner.

The accompanying continuation application is filed in response to an Office Action mailed July 17, 2001 and an Advisory Action mailed January 3, 2002 in the parent application 09/083,290. Applicants respectfully request reconsideration of this application in view of the following remarks. The accompanying November 18, 2001 Declaration of Dr. Heidi Stuhlmann with an attached manuscript is offered as additional support for Applicants' invention.

Claims 1-6 are pending. Claims 7-25 have been cancelled without prejudice to the prosecution of this subject matter in separate patent applications. Applicants submit this Preliminary Amendment to continue prosecution of claims 1-6 in the instant application.

Applicants amended the specification to provide a cross-reference to related application section and to specify Applicants' claim of priority to prior continued prosecution application (CPA) filed July 5, 2001 of application Serial No. 09/083,290 filed May 22, 1998.

In the parent application the Examiner rejected pending Claims 1-6 under 35 U.S.C. §101 as unpatentable due to lack of utility. Applicants have argued that the legal standard of utility has been satisfied for the following reasons:

The Examiner asserts that *Vezf1* homology to DB1 gene does not suggest any utility for *Vezf1*, since the function of DB1 protein was unknown at the time of invention. The Examiner also asserts that function of the *Vezf1* protein is not disclosed in the specification or the art. The Examiner contends that *Vezf1* mRNA expression during angiogenesis does not indicate a function for the protein, because the specification does not teach that the *Vezf1* gene is specific to vascular disorders or endothelial cells. Furthermore, the Examiner indicates that *Vezf1* expression is not limited to expression during angiogenesis and therefore cannot be used to mark cells undergoing angiogenesis.

An invention has a well-established utility if (1) a person of ordinary skill in the art would immediately appreciate that the invention is useful based on the characteristics of the invention (e.g. properties or application of a product or process), and (2) the utility is specific, substantial and credible. Furthermore, an applicant need only provide one credible assertion of specific and substantial utility for each claimed invention to satisfy the utility requirement.

First, the Examiner appears to be misguided by the Applicant's comparison of *Vezf1* to DB1 (specification page 6, line 15 to page 7, line 3). It is provided merely as an

example of a identified gene, that possessed 98% sequence homology with *Vezf1*. The fact that DB1 had no identified function at the time of the invention has no bearing on the utility of *Vezf1*.

Applicants disagree with the Examiner's contention that the specification does not disclose a function for *Vezf1* gene products. The specification outlines multiple uses for *Vezf1* gene products. They include the use of *Vezf1* as an endothelial cell marker (page 7, lines 11-13), its use in the development of animal models for angiogenesis (page 8, lines 1-6), its use as a diagnostic tool for vascular disorders (page 7, lines 14-21), and its use in the treatment of vascular disorders (page 8, lines 7-11). These uses described above are supported by the pattern of *Vezf1* expression in proliferating endothelial cells found in capillary networks and mature vessels. Therefore, the Applicants submit that the present invention provides sufficient examples to satisfy the requirement for specific utility.

The contents of Declaration of Dr. Heidi Stuhlmann provide substantial support for *Vezf1* as a marker for vascular endothelial cell proliferation. *Vezf1* mRNA expression localizes to populations of endothelial cells found in capillary networks in both normal and pathological states. It is highly specific to endothelial cells of capillaries and mature vessels in muscle, skeletal, lung, liver, kidney, bone marrow and heart tissue. Expression of *Vezf1* in capillaries found within induced tumors, human breast tumors, and human atherosclerotic plaques are an strong indications that *Vezf1* gene products have specific and functional roles in regulating angiogenesis. Furthermore, injury-induced proliferation of endothelial cells in rat aortas also stimulates *Vezf1* upregulation. This expression was low, but detectable in untreated arteries, became intense at 2 weeks post-injury in treated arteries, and decreased at 4 and 6 weeks post-injury in treated arteries.

The spatial and temporal correlation of *Vezf1* expression with proliferating endothelial cells within injured arteries demonstrate a specific function that is limited to angiogenic activity. Specific *Vezf1* expression during endothelial cell proliferation demonstrates that it can be used as a marker for angiogenesis. Furthermore, association with pathological endothelial cell proliferation provides the basis for practical or real world benefits. Therefore, the Applicants submit that the present invention satisfies the requirement for substantial utility.

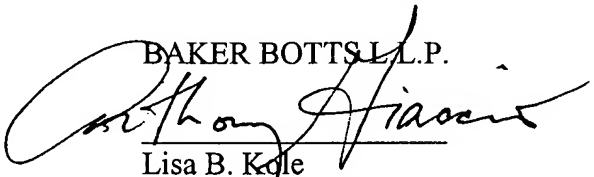
The Applicants also contend that a person of ordinary skill in the art would immediately appreciate that the present invention is useful based on the expression pattern of *Vezf1* and that the present invention satisfies the requirement for credible utility under 35 U.S.C. §101.

Conclusion

In view of the above remarks and the enclosed Declaration, the Applicants submit that claims 1-6 constitute allowable subject matter. A Notice of Allowance is respectfully requested.

Respectfully submitted,

BAKER BOTTS L.L.P.



Lisa B. Kole
PTO Reg. No. 35,225

Anthony Giaccio
PTO Reg. No. 39,684

ATTORNEYS FOR APPLICANTS
(212) 408 2568

MARKED UP VERSION OF AMENDMENT

Amendments to the paragraph beginning on page 14, line 16 and ending on page 15, line 2:

Two purified and isolated nucleic acids, together comprising *Vezf1* cDNA, termed *mVezf1.1* (3-1444) and *mVezf1.2*(1394-2820), containing nucleic acid residues 3-1444 (in a 1.444 kb EcoRI-EcoRI cDNA fragment) and 1394-2820 (in a 1.429 kb EcoRI-EcoRI cDNA fragment) of murine *Vezf1* cDNA, respectively, in pBluescript II SK (grown in DH5ÿ) and a nucleic acid, termed *mVezf1.N*, containing the aforementioned 20 kb genomic NotI-NotI fragment in pBluescript II SK (grown in DH5ÿ) , have been deposited under the terms of the Budapest Treaty with the American Type Culture Collection (ATCC), having an address of 12301 Parklawn Drive, Rockville, Maryland, 20852 on May 19, 1998 and assigned accession nos. 209873, 209874, and 209875 respectively.

ATCC

10801 University Blvd • Manassas, VA 20110-2209 • Telephone: 703-365-2700 • FAX: 703-

BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF
THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

INTERNATIONAL FORM

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT ISSUED PURSUANT TO RULE 7.3
AND VIABILITY STATEMENT ISSUED PURSUANT TO RULE 10.2

To: (Name and Address of Depositor or Attorney)

Brookdale Center for Development and Molecular Biology
Mount Sinai School of Medicine
Attn: Heidi Stuhlmann, Ph.D.
Box 1126
New York, NY 10029

Deposited on Behalf of: Mount Sinai School of Medicine

Identification Reference by Depositor:	**ATCC Designation**
Plasmid DNA mVezf1.1	209873
Plasmid DNA mVezf1.2	209874
Plasmid DNA mVezf1.N	209875

The deposits were accompanied by: ___ a scientific description _ a proposed taxonomic description indicated above. The deposits were received May 19, 1998 by this International Depository Authority and have been accepted.

AT YOUR REQUEST: X We will inform you of requests for the strains for 30 years.

The strains will be made available if a patent office signatory to the Budapest Treaty certifies one's right to receive, or if a U.S. Patent is issued citing the strains, and ATCC is instructed by the United States Patent & Trademark Office or the depositor to release said strains.

If the cultures should die or be destroyed during the effective term of the deposit, it shall be your responsibility to replace them with living cultures of the same.

The strains will be maintained for a period of at least 30 years from date of deposit, or five years after the most recent request for a sample, whichever is longer. The United States and many other countries are signatory to the Budapest Treaty.

The viability of the cultures cited above was tested June 10, 1998. On that date, the cultures were viable.

International Depository Authority: American Type Culture Collection, Manassas, VA 20110-2209 USA.

Signature of person having authority to represent ATCC:

Barbara M. Hailey

Barbara M. Hailey, Administrator, Patent Depository

Date: June 24, 1998

cc: Dr. Lisa Kole, Esq. (Ref. Docket 970901)